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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PATTERSON, CHARLES L JR	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/908,943	YAN ET AL.	
	Examiner	Art Unit	
	Charles L. Patterson, Jr.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2003 and 27 May 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,23 and 25-101* is/are pending in the application.

4a) Of the above claim(s) *1-20,28-82 and 96-101* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,23,25-27 and 83-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The examiner agreed to do a non-final rejection after carefully considering applicants argument in the interview of 11/21/03. After carefully reviewing the case file and the last action, this action is being done. It supercedes the outstanding final rejection.

New claims 96-101 were restricted out as groups 28, 30-32, 37 and 50 in the previous restriction requirement. Therefore these claims will not be examined here. Claims 1-20, 28-82 and 96-101 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Claims 21 and 89 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant two claims are confusing because they are apparently identical in scope, with only a few words changed and P_1 and P_2 exchanged.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 23, 25-27, 84 and 86-95 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The instant claims now are drawn to peptides "having 4 to 50 amino acids" or "having 6 to 50 amino acids". Applicants do not point out where there is enablement for these limitations in the specification and the examiner has been unable to find these limitations in the specification. On page 7, lines 2-22 it is taught that in fusion polypeptides "the linker may be a peptide linker comprising about 20 to about 40 amino acids" and on page 33, lines 18-20 it is taught that "the distance between the cleavage site and the start of a transmembrane domain is about 20-40 amino acids in order to mimic the steric properties of the APP β secretase cleavage domain". On page 88, lines 9-13 it is taught that a fusion protein with a maltose binding protein and 125 amino acids from APP C-terminus was produced. None of these recitations teach the limitations of 4-50 or 6-50 amino acids in the instant claims. Absent a convincing showing that these limitation are taught in the instant specification, they must be removed from the instant claims.

Claims 21, 23, 25-27 and 83-95 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that the specification teaches the need to identify surrogate substrates for the human aspartyl protease (Hu-Asp2) and that of "the peptide substrates that were most 'effective Hu-Asp2 substrates. Thy/Phe

and Leu were the most abundant amino acids at the P_1 site; Asn appeared several times at the P_2 site; Glu, Asp, and Ala were prominent in the P_1'; Val occurred frequently in the P_2'; the sequence Glu-Val-Glu appeared at the $P_1'P_2'P_3'$ of ubiquitin, another Asp2 substrate'" and that "[u]sing these observations the inventors designed exemplary peptides such as those presented in Table 2". They further argue that "[t]he enablement requirement...requires only that the specification provides a teaching of how one of skill in the art could make the invention and how one of skill in the art should use the claimed invention...[and that] the specification explicitly teaches one skilled in the art how to produce peptides comprising specific sequences as artificial substrates for Hu-Asp2". They further argue that "[t]he facts of the present case are akin to the facts of *In re Wands*" in that the question of undue experimentation is involved. It is argued that "the present application provides numerous working examples of peptide substrates of Hu-Asp2...[and that] it would be routine experimentation to generate substrates contemplated by the present invention".

The examiner does not agree. To start with, the majority of the claims are now limited to peptides 4-50 or 6-50 amino acids long. As discussed *supra*, this embodiment is apparently not disclosed in the instant specification. The embodiments of the claims, even with this limitation, are very broad and have innumerable possibilities. Just because Tyr, Phe and Leu were the most abundant amino acids at the P_1 site, Asn appeared several times at the P_2 site, Glu, Asp, and Ala were prominent in the P_1', Val occurred frequently in the P_2' site does not necessarily mean that a rule can be made as in claims 21, 27, 83 and 89 as to the cleavage sites. Just because certain amino acids were "the most abundant", "appeared several times", were prominent, and "occurred frequently" at particular positions does not mean that

applicants can make a general rule using these findings. How the residues relate to others around them has to be taken into account. Without an assay for activity one of ordinary skill would not know which were substrates and which were not. None of the claims are limited to the sequences in Table 2, for instance, but are drawn to a much broader general formula. All or even a significant number of the embodiments of this formula have not been shown to be substrates. As to *In re Wands*, this case involved assaying an antibody against hepatitis B-surface antigen. The case did not involve a general formula comprising numerous possibilities as is the case here. Therefore the rejection is maintained.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21, 23, 25-27, 83-85 and 89 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Sano, et al. (A). The instant reference teaches in SEQ ID NO:4 the sequence Asp-Tyr-Asp-Ala in residues 10-13. The peptide is 20 amino acids

long. The patent office does not have the facilities to test the instant peptides to see if the proteases of the instant claims will cleave this peptide or whether it may contain a transmembrane domain, but absent convincing proof to the contrary it is maintained it does. The addition of a label to aid in the assay would have been obvious. This rejection is being done under 102/103 since it is not known whether the peptides are cleaved by the proteases, but since they meet the requirements of the instant claims as to sequence it is maintained that they are.

Claims 83 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Semerjian, et al. (U), Van Camp, et al. (V), Lowell, et al. (W) or Sellar, et al. (X). The references have been characterized in the previous action. It would have been obvious to use a detectable label and a quenching moiety in the peptide in view of the general knowledge of one of ordinary skill in the art. The motivation would have been to readily measure the cleavage of the substrate. The cleavage rate of Hu-Asp2 on the instant substrates is not known but since the reference meets the requirement of claim 83, it is presumed that this rate is as in claim 85, absent convincing proof to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone number is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
December 9, 2003